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Original Research Article

Retinopathy of prematurity: screening programme for preterm infants in Ondo State, South-West, Nigeria

Stella A. Adegbehingbe[1], Rosena O. Oluwafemi[2]*

[1]Department of Ophthalmology, University of Medical Sciences Teaching Hospital, Akure, Nigeria
[2]Department of Paediatrics and Child Health, University of Medical Sciences Teaching Hospital, Akure, Nigeria

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***Correspondence:**
Dr. Rosena O. Oluwafemi,
E-mail: bankyfem@yahoo.com

ABSTRACT

Background: Retinopathy of prematurity (ROP) is one of the avoidable causes of childhood blindness in the whole world. The disease can be mild, it can resolve spontaneously, and it could also have a grave consequence of blindness. As such, all extreme and very preterm babies at risk for ROP and having additional systemic co-morbidities and risk factors must be screened.
Methods: Preterm babies with gestational age up to 32 weeks and birth weight less than 1500 g were prospectively recruited into the study. Retinal examination using binocular indirect ophthalmoscope with +20DS lens was done at 4 to 6 weeks post-delivery and were subsequently followed up. Data were analyzed using the software package for social science (SPSS) version 20.0 Categorized data were presented as percentages, p value <0.05 was considered significant.
Results: Fifty-two preterm babies with birth weight ranging between 900-1500 g and gestational age ranging between 26-32 weeks were examined. ROP was detected in 7 babies (13.5%), Four (57.1%) babies had stage 1 ROP, 3 (42.9%) had stage 2 disease and none had stage 3 disease. ROP was commoner in the female babies 6 (86%). Neonatal sepsis and use of up to 3-days supplemental oxygen therapy (p=0.024) were the only risk factors associated with all the babies with ROP in the study.
Conclusions: Prevalence of ROP was 13.5% in the current study with risk factors of neonatal sepsis and use of supplemental oxygen of up to 72 hours post-natal life.

Keywords: ROP, Prematurity, Prevalence, Ondo State

INTRODUCTION

Retinopathy of prematurity (ROP) or Terry syndrome, previously known as retrolental fibroplasia (RLF), is a vaso-proliferative disease of the retina affecting eyes of the preterm babies.[1] The retina is a distinctive tissue that has no blood vessels until the fourth month of gestation.[2] The vessels growth is complete in the nasal periphery by eight month of gestation and in the temporal periphery by one month after delivery. Therefore, vascular development is disrupted early in infants born preterm and at extremely low gestational ages (GA).[3] Preterm birth removes the visual system from the nurturing intrauterine environment during a period of rapid maturation, thus the risk of reduced visual function is increased.[4] This makes preterm babies to be more prone to visual impairments than term babies. About 32,300 infants worldwide are diagnosed with irreversible vision impairment due to ROP yearly, of which about 20,000 become blind or have severe visual impairment.[4] Preterm babies receiving intensive neonatal care, in which oxygen therapy is used on them due to the immaturity of their lungs are at risk of developing ROP. There is evidence that the population of preterm infants at risk of severe ROP varies depending on the level of neonatal intensive care received.[5] However, despite advances in neonatal care, the occurrence of ROP and associated complications with associated visual

impairment has been increasing and remains difficult to control.[6]

In countries like America and western Europe with high development indices and very low neonatal mortality rates, severe ROP is generally limited to extremely preterm infants, that is, babies weighing less than 1000 g at birth.[3] At the other end of the development spectrum, countries with very low development indices and very high neonatal mortality rates in the sub-Saharan Africa, ROP is rare as most preterm babies do not have access to neonatal intensive care and may not survive.[7] However, with the advent of advances in neonatal care in the special care baby unit (SCBU) of our health facilities more preterm babies are surviving.[8] This has necessitated the need for examining the preterm babies for ROP especially with the use of supplemental oxygen or those with other associated risk factors such as sepsis, jaundice, blood transfusion and various other co-morbidities.

METHODS

Study area

The study was carried out at the Mother and Child Hospital, Akure (MCHA). It is a very busy purpose-built 100-bedded (60 obstetrics and 40 paediatric beds), public facility and referral centre providing specialized health care services to the state capital and surrounding communities. The average delivery rate was 4000 babies per annum, with preterm babies accounting for approximately 15%.[8] There is no restriction on the type of cases admitted into this facility. Thus both booked and non-booked women were accepted for elective or emergency delivery. Akure is the Capital of Ondo State, located in the South-West geo-political zone of Nigeria with a land expanse of 15,000 square kilometers.

Study design

This was a prospective study, ethical clearance was obtained from the research and ethics committee of the MCHA and verbal informed consent taken from mothers of the babies. The participants were all preterm babies delivered, managed and followed up in the specialty clinic of the health facility from May 2016 to May 2017.

Data collection

The babies were recruited from the in-born part of the special care baby unit (SCBU) of the Hospital. Babies' gestational age were confirmed using the new Ballard's chart, birth weight was taken using the RGZ-20 weighing scale. The scale records weights in grams to the nearest 25 g. It was usually adjusted for zero error before each reading. Other measures taken to ensure reliability of results included weekly standardization of the weighing scale, using known weights. Babies who meet the inclusion criteria and other risk factors such as use of supplemental oxygen, sepsis, respiratory distress syndrome (RDS), anaemia with multiple blood transfusions, intra-ventricular haemorrhage (IVH), use of phototherapy, multiple gestation, gender and antenatal corticosteroid use, were recruited.

Inclusion criteria

Inclusion criteria that qualify the baby for ROP screening included: Infants with a birth weight of <1500 grams, infants with an estimated gestational age at birth of <32 weeks and infants who do not meet the first two criteria but are deemed at high risk by the neonatologist due to other medical conditions.

Exclusion criteria

Non-consenting mother were excluded from the study.

Sample size calculation

About 20 preterm babies are born per month (240 per annum) in our centre and a previous study done in the centre reported 15.4% prematurity rate, of which the very preterm were 7.7%.[8] We used 15% of 240 and a value of 36 was obtained which was rounded up to 52 for the purpose of adequacy and accuracy.

Timing of the first ROP examination

For infant born at ≤27 weeks gestation, first eye exam was done at 31 weeks postmenstrual age (gestation age at birth + chronological age) and for infants born at >27 weeks gestation, first eye exam was at 4 weeks chronological age.

ROP follow-up examinations

The babies with no disease were re-examined approximately every two weeks until vascularized in zone III. Babies with mild disease (stage 1 or stage 2, zone II) were examined every one to two weeks until regressed. Babies with pre-threshold (zone I disease any stage; zone 2 with stage 2 and plus, or stage 3) were examined every two to seven days until regressed. Babies with regressing ROP were examined two to eight week intervals until stable and long term follow up occurred at regular neonatology clinic.

ROP screening

The ocular examination which included the external eye, anterior and posterior segments was carried out. It was a weekly visit to the SCBU and the neonatal clinic. The external and anterior segments were examined using a pen torch. To examine the posterior segment, the pupils were dilated using eye drops; 2.5% phenylephrine and 0.5% tropicamide combination eye drops were instilled. One drop, with 2 instillations at 5 minutes apart were dropped into the inferior fornices of the babies and the excess drops was wiped off. Pupils were checked after 20 minutes for pupillary dilatation. Maximum pupillary dilatation was

achieved between 30–45 minutes after which fundus examination was performed. Additional eye drop was instilled if there is insufficient pupillary dilatation. The eyelids were gently pulled apart with a pediatric reusable eye lid speculum after application of topical anaesthetic agent (1% proparacaine). Binocular indirect ophthalmoscope with a Volk +20D lens was used to examine the fundi after complete pupillary dilatation by the ophthalmologist experienced in ROP screening. The cornea was kept moist during the examination by instilling intermittent drops of topical balanced salt solution. The eyeball was rotated with a cotton bud to view the temporal and nasal retina periphery.

ROP staging

The retinal findings were recorded for each eye according to the international committee for classification of ROP (ICROP).[9] Classification was based on the most advanced stage of ROP in the eyes of a baby. Babies with ROP had screening examination weekly to monitor the progression or regression. Babies who required repeat examination and have been discharged were examined on an outpatient basis at the neonatal clinic. The study protocol adhered to the tenets of the Declaration of Helsinki. Babies' demographic characteristics as well information on gestational age at birth, birth weight, oxygen therapy, and presence of other risk factors were retrieved from their hospital records.

Data analysis

The data were entered into an excel sheet and later analyzed using the software package for social science (SPSS) version 20.0 (Windows Inc; Chicago, IL, USA). Categorized data were presented as percentages, p value <0.05 was considered significant.

RESULTS

A total of 52 preterm babies were screened during the study period. There were 23 males (44.2%) and 29 females (55.8%) giving a male to female ratio of 0.8:1. The mean birth weight was 1215.38 g with a range of 900 g to 1,500 g. The mean GA at birth was 29.65 weeks with a range of 26 to 32 weeks, Forty-seven (90.4%) were hospital deliveries while 5 (9.6%) were non-hospital deliveries, 14 (26.9%) babies were products of multiple gestation and 23 (44.2) of the babies belong to the middle socioeconomic status (Table 1).

Table 2 showed the characteristics of the mother of the babies, majority of the mothers were in the age range of 20 to 39 years, one was a teenager and 7 (13.5%) were ≥40 years. Eighteen (34.6%) of the mothers received antenatal corticosteroids, 21 (40.4%) of the mothers were civil servants and 33 (65.5%) had tertiary education.

Table 1: General characteristics of the babies.

Characteristics	Frequency	Percentage
Birth weight (g)		
Extreme low (<1000)	13	25.0
Very low (<1500)	39	75.0
Total	52	100.0
Gestational age (weeks)		
Extreme preterm (<28)	8	15.4
Very preterm (28-32)	44	84.6
Gender		
Male	23	44.2
Female	29	55.8
Place of delivery		
Hospital	47	90.4
Non-hospital	5	9.6
Total	52	100.0
Products of multiple gestation		
Yes	14	26.9
No	38	73.1
Total	52	100.0
Socio-economic class		
Lower	21	40.4
Middle	23	44.2
Upper	8	15.4
Total	52	100

Table 2: Characteristics of mothers of the babies.

Characteristics	Frequency	Percentage
Maternal age (years)		
<20	1	1.9
20-24	12	23.1
25-29	10	19.2
30-34	14	26.9
35-39	8	15.4
≥40	7	13.5
Total	52	100.0
Antenatal use of steroids		
Yes	18	34.6
No	34	65.4
Total	52	100
Maternal occupation		
Artisan	13	25.0
Civil servant	21	40.4
Cleaner	2	3.8
Housewife	4	7.7
Trader	12	23.1
Total	52	100
Level of education		
Primary	2	3.8
Secondary	17	32.6
Tertiary	33	65.5
Total	52	100

There were various indications for preterm delivery which includes eclampsia (3.8%), severe pre-eclampsia (1.9%), antepartum haemorrhage (1.9%), premature rupture of membrane/previous caesarian section (1.9%), cervical dystocia (1.9%), fetal distress (3.8%), breech (3.8%) and 42 (80.8%) of the mothers had spontaneous vaginal delivery (80.8%) while emergency caesarian section occurred in eight mothers (15.4%) and two mothers (3.8%) had elective caesarian section (Table 3).

Table 3: Reasons for prematurity.

Mode of delivery/indication	Frequ-ency	Percen-tage
ELLCS for Breech	2	3.8
EMLSC for APH (PP)	1	1.9
EMLSCS for cervical dystocia	1	1.9
EMLSCS for eclampsia	2	3.8
EMLSCS for fetal distress	2	3.8
EMLSCS for PROM and previous CS	1	1.9
EMLSCS for severe pre-eclampsia	1	1.9
Spontaneous vaginal delivery	42	80.8
Total	52	100.0

ELLCS: elective caesarean section, EMLSCS: emergency lower segment caesarean section, APH (PP): antepartum haemorrhage (placenta previa), PROM: preterm rupture of membranes

All the babies had systemic co-morbidities and received different treatment interventions. They all had supplemental oxygen, but the duration differed. Twelve (23.1%) received supplemental oxygen for 24 hours while ten babies (19.2%) had supplemental oxygen for 7-15 days. Thirty-nine (75%) received aminophylline, forty-eight (92.3%) had phototherapy. Anaemia was found in twenty-five (48.1%) of the babies and they were transfused with blood. Two babies (3.9%) had mild to moderate conjunctivitis (ophthalmia neonatorum) (Table 4). Table 5 showed the characteristics of the seven babies (13.5%) of the 52 with ROP. ROP was more common in females, 6 (86%) while there was only one male (14%) with the disease. In terms of severity, four (57.1%) babies had stage 1 ROP, three (42.9%) had stage 2 disease. None of the infants examined had stage 3, 4 or 5 ROP. All babies were observed, and subsequent retinal examinations showed regression of ROP. All the babies with ROP had neonatal sepsis (100%) as co-morbidity, 28.6% had apnoeic episodes while 14.3% had respiratory distress, plethora, hypothermia, anaemia, and neonatal jaundice (Table 4).

Table 4: Co-morbidities and treatment interventions received by babies.

Co-morbidities and treatment interventions	Frequ-ency	Percen-tage
Co-morbidities		
Neonatal sepsis	12	9.6
Respiratory distress syndrome	39	75.0
Neonatal jaundice	48	92.3
Plethora	5	5.8
Hypothermia	13	3.8
Apnoeic spells and cardiac murmurs	3	3.8
Foetal asphyxia	2	1.9
Hypoglycemia	4	1.9
Anaemia	25	48.1
Ophthalmia neonatorum	2	3.8
Treatment interventions received		
Supplemental oxygen therapy	52	100.0
Phototherapy	48	92.3
Use of aminophylline	39	75.0
Blood transfusion	25	48.1

Table 5 showed the characteristics of the seven infants who had ROP. All of them were 30 weeks and below, the birth weights were also less than 1,500g except one whose weight was 1,500 g. Five (71.4%) of them had oxygen therapy for 72 hours and less while two babies (28.6 %) had oxygen therapy for more than 72 hours. The 3 day-oxygen therapy is significantly associated with incidence of ROP (X^2=11.269, p=0.024). Table 6 showed that higher duration on oxygen was significantly associated with incidence of ROP (t=2.90, p=0.004) and lower duration of oxygen therapy was significantly associated with absence of ROP meanwhile mean birth weight of the infants who had ROP was 1256.25 (±25 g) compared with 1244.0 (±24) g for ROP-free infants (p=0.048). In addition, the mean gestational age of ROP infants was 30.1 (±1.0) weeks compared with 29.6 (±1.02) weeks for ROP-free infants (p=0.004).

Table 5: Characteristics of the seven infants who had ROP and their duration of oxygen therapy.

Infant	Gestation	GA (weeks)	ROP staging	BW (g)	Sex	Duration on oxygen
1	Single	30	1	1200	F	72 hours
2	Twin	28	2	1000	F	14 days
3	Single	30	1	1500	F	72 hours
4	Single	30	1	1300	F	48 hours
5	Single	30	1	1300	F	24 hours
6	Twin	28	2	1000	F	10 days
7	Twin	30	1	1250	M	72 hours

X^2=11.269, p=0.024), GA: gestational age, ROP: retinopathy of prematurity, BW: birth weight

Table 6: Comparison of gestational age, birth weight and duration on oxygen across ROP and ROP-free babies.

Variables	Babies with ROP (mean±SD)	Babies without ROP (mean±SD)
GA (weeks)	30.125±1.00	29.568±1.02
Birth weight (g)	1256.25±250	1244±235
Duration on oxygen (hours)	114.00±2.00	99.40±1.00
	t=2.90, p=0.004*	t=1.98, p=0.048*

*GA: Gestational age, G: grams

DISCUSSION

The incidence of ROP in this study was 13.5%, of which 57.1% had stage 1 ROP and 42.9% had stage 2 disease. The incidence of ROP in this study is similar to 13.7% that was reported from Ghana, 12.2% from Ibadan, Nigeria and 15% from Lagos, Nigeria.[10-12] However, it is much less than reports from Calabar, Nigeria (21%), Iran (30%), Kenya (41.7%) and Port Harcourt, Nigeria (47.2%).[13-16] These differences could be due to regional variations or disparities in the sample size. More research from neonatal units in different parts of the country may be required. There seems to be an increase in ROP cases detected in Nigeria. This may not be unconnected with the fact that there are more screening centres as more ophthalmologists are getting trained in the management of ROP. This has also contributed to the increase in awareness about ROP.[17] While the opposite seems to be the order of the day in developed countries where ROP is found to be declining probably due to the advancement in neonatal care and screening.[18]

The well recognized risk factors for ROP such as respiratory distress, anaemia, apnoeic episodes, sepsis, administration of blood transfusion and multiple gestation were all present in the babies in the current study. Moreover, all the babies who had ROP had neonatal sepsis and at least 3 day-oxygen therapy which was significantly associated with ROP. This is similar to the Port Harcourt study that found supplemental oxygen, sepsis and anemia needing blood transfusion to be significantly associated with incidence of ROP.[16] This is at variance with the Ibadan and Calabar studies which did not find any association between these risk factors.[11,13] Only necrotizing enterocolitis was significantly associated with ROP in the Ibadan study.[11] The quality of neonatal service, sample size and the fact that this is the first ROP screening at our centre may be responsible.

The mean gestational age (±SD) and birth weight (±SD) for babies with ROP were slightly higher than for those without ROP but when oxygen therapy was factored in, the babies with higher duration on oxygen were significantly more affected with ROP and lower duration of oxygen therapy was significantly associated with absence of ROP. This is in contrast to what was obtained in Calabar, Port Harcourt, and Lagos studies where ROP were inversely associated with gestational age and birth weight.[12-14] Our finding is however similar to the report from Ibadan New York and India where ROP was detected more in older preterm babies.[11,19,20] These findings suggests that there may be other contributory factors to the occurrence of ROP other than the known risk factors. And that more studies are needed in our environment so as to identify our own peculiarities, risk factors and to establish screening criteria. Among the seven preterm babies who had ROP, four of them had stage 1 disease (57.1%) while the remaining three babies had stage 2 disease (42.9%). Stage 1 ROP was more than stage 2 ROP which is similar to Port Harcourt and Calabar studies but at variance to Ibadan study where the highest numbers of ROP was stage 2 disease. Stages 3, 4 or 5 ROP were not detected in this study as in Calabar study and similar to Ibadan and Port Harcourt in which there were no stages 4 and 5 diseases. This may be due to at risk babies dying before eye examination or being too sick to undergo eye examinations. There were more females than male (6:1) affected with ROP, similar to Calabar study but in contrast to Port Harcourt which reported a higher male preponderance. The reason for this may be the variation in the sample sizes of the various studies. Three of the babies with ROP in this study were of twin gestation which is also similar to the Calabar study which had fewer of preterm babies with multiple birth having ROP than those with singleton birth.

Limitations

Prior to this time, there was no ROP screening programme in Ondo state. There is also paucity of the relevant medical staff who are specifically trained to carry out the programme in the state (both among ophthalmologists and the neonatologists). This study is nouvelle in Ondo state and it will definitely be improved upon.

CONCLUSION

The prevalence of ROP in the current study is high. ROP is a hidden disease and its detection will only increase with increasing screening for the disease. Improvement in neonatal care will result in survival of more preterm babies who are entitled to quality life hence there is need for an increase in awareness and screening programmes in our health facilities to enhance prompt detection and timely treatment to prevent blindness.

Recommendations

The prevalence of ROP was 13.5% in the current study, this is high. A screening program needs to be developed with standardization as it is becoming clearer that the disease may not be rare in Africans as previously thought. Better and more advanced care are evolving in our health facilities hence essential resources for imaging and

treatment are needed to be established for a successful screening program.

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